Mammary analogue secretory carcinoma: A case report

Carcinome sécrétoire analogue mammaire: à propos d'un cas

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RÉSUMÉ

Introduction: Le carcinome sécrétoire analogue mammaire est une nouvelle entité rare de tumeur maligne de bas grade des glandes salivaires. Elle presentait les mêmes caractéristiques histologiques et la translocation chromosomique t (12; 15) (p13; q25) que celles du carcinome sécrétoire du sein.

Objectif: Mettre en évidence les approches diagnostiques et la prise en charge de cette tumeur qui est le premier cas rapporté en Tunisie.

Observation: Un cas de MASC de la muqueuse jugale inférieure gauche a été examiné pour ses caractéristiques microscopiques et immunohistochimiques. L'hybridation in situ par fluorescence (FISH) pour la translocation ETV6 – NTRK3 a été réalisée. La chirurgie était le seul traitement opté dans ce cas. Aucun signe de récidive locale ou régionale au cours du suivi d'un an n'a été observé.

Commentaires: Le carcinome de sécrétion a été confondu avec d'autres tumeurs des glandes salivaires, en particulier le carcinome à cellules acineuses, en raison de leurs similitudes morphologiques, rendant le diagnostic difficile. L'hybridation in situ en fluorescence (FISH) est le résultat définitif permettant de confirmer le diagnostic de MASC et de le différencier des autres types de tumeurs des glandes salivaires. À l'heure actuelle, aucun traitement spécifique n'est disponible pour les patients atteints de MASC.

Mot clés : glande salivaire, carcinome sécrétoire, carcinome à cellules acineuses, carcinome sécrétoire analogue mammaire, translocation ETV6-NTRK3, mammaglobine, S100, DOG1

SUMMARY

Background: Mammary analogue secretory carcinoma is a rare new entity of low-grade malignant tumor of salivary glands. It shared the same histologic features and the chromosomal translocation t(12;15)(p13;q25) as secretory carcinoma of the breast.

Aim: To highlight the diagnosis approaches and the attitude of management in a case of MASC which is the first case reported in Tunisia.

Reported case: A case of MASC of the lower left jugal mucosa was reviewed for its microscopic and immunohistochemical features. Fluorescence in situ hybridization (FISH) for the ETV6–NTRK3 translocation was performed. Surgery was the only treatment required in this case. No signs of local or regional recurrence during the one-year follow-up were noticed.

Commentaries: Secretory carcinoma was confused with other salivary gland tumors especially acinic cell carcinoma due to their morphological similarities, making diagnosis dilemma. Fluorescence in-situ hybridization (FISH) is the one definitive finding to confirm the diagnosis of MASC and to differentiate it from the other types of salivary gland tumor. At the present time, no specific therapy is available for patients with MASC.

Key words: salivary gland, secretory carcinoma, acinic cell carcinoma, mammary analog secretory carcinoma, ETV6-NTRK3 translocation, mammaglobin, S100, DOG1.

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INTRODUCTION

Mammary analogue secretory carcinoma (MASC) is a recently described salivary gland malignancy which was first reported by Skálová et al. in 2010.as it shared the same histologic features and the chromosomal translocation t(12;15)(p13;q25) as secretory carcinoma of the breast (1). Since the first description of MASC, several reviews and more than 232 additional cases have been reported discussing the histological, immunohistochemical and genetic aspects of this neoplasm. MASC was most commonly misdiagnosed as acinic cell carcinoma (AciCCs).and was confused with other salivary gland tumors due to their morphological similarities, making diagnosis dilemma (2) Immunohistochemical and molecular analysis represents the key diagnostic tests for secretory carcinoma.

In this paper we highlighted our diagnosis approaches and our attitude of management in this case of MASC which according to our knowledge is the first case reported in Tunisia.

REPORTED CASE

It is a case of 33-year-old man with no relevant medical history, complaining of a 15mm, well limited, soft and fluctuant nodule in his lower left jugal mucosa. The lesion was excised and it was diagnosed as a mucocele.

After three years, the patient came back with a 15mm scar appearance lesion, in the same location centered by asymptomatic, firm, well limited, mobile 7mm*7mm nodule which appeared in the submucosa, involving for four months with no palpable lymphadenopathy. The preoperative diagnosis was a benign tumor of minor gland salivary.

The lesion was excised and grossly the specimen consisted of a 5mm*5mm nodule of bluish soft tissue that exuded a translucent yellowish gel from the center when bisected with focal extension to the adjacent tissues. The specimen was strongly suggestive of a minor gland salivary neoplasm so a wedge excision of the scar with a 1cm margin has been accomplished.

Histopathological analysis showed a circumscribed papillary cystic and microcystic growth. The tumor cells had a well-developed eosinophilic cytoplasm and low-grade vesicular nuclei with finely granular chromatin distribution but with no prominent atypia or mitoses. No evidence of perineural invasion was identified. The periodic acid- Sciff (PAS) was negative. The margins of the specimen were invaded on histopathological analysis despite the impression of macroscopic clearance at operation. Anatomopathological studies evoked the diagnosis of acinic cell carcinoma. Afterwards immunohistochemical analysis was performed and had stained for S100, mammaglobin and CK19. It did not stain for DOG1. The diagnosis of MASC was made. Fluorescent insitu hybridization analysis confirmed the diagnosis by showing rearrangement of the ETV6 gene.

The patient was scheduled for CT scan which revealed no evidence of metastases and for MRI image which showed a 1.5cm*1.5cm T1 gadolinium enhancing.

Facing the clinical context, a surgical revision was performed. The histopathological analysis showed an inflammatory infiltrate with no residual tumor. Neither chemotherapy nor local radiation therapy was required.

The patient had no signs of local or regional recurrence during the one year follow-up.

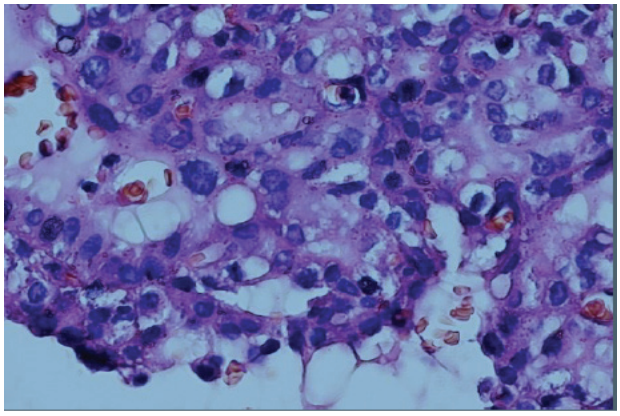

Figure 1. MASC tumor cells with eosinophilic cytoplasm and low-grade vesicular nuclei (H&E ×400)

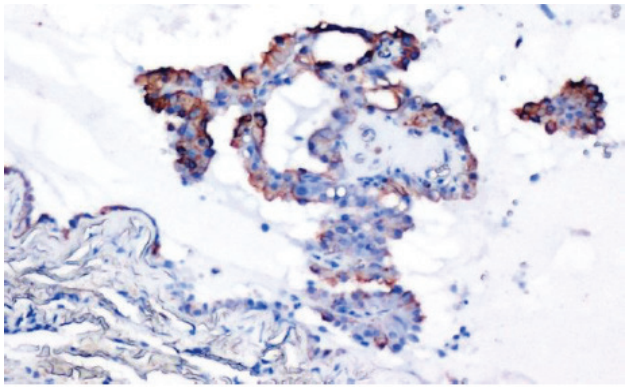

Figure 2. CK19 protein staining is present in the tumor cells (magnification ×100)

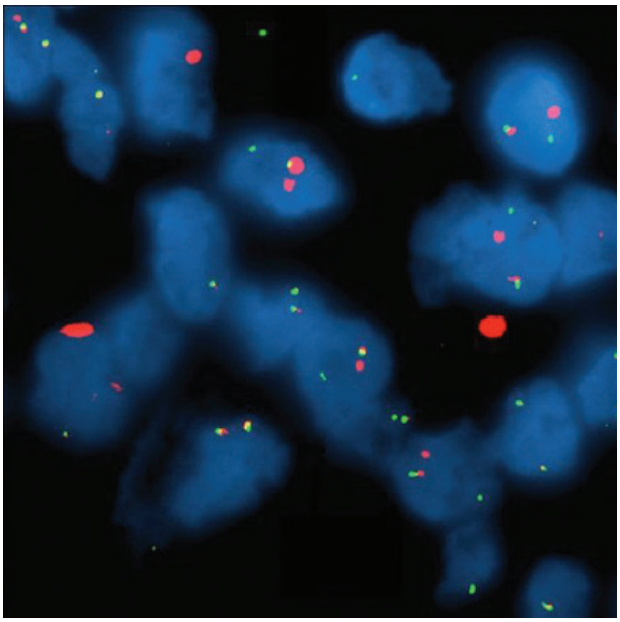

Figure 3. FISH analysis reveal rearranged ETV6 gene. Yellow (red/green fusion) signal demonstrates intact chromosome, separated red and green signals mean gene break.

DISCUSSION

This work describes the diagnosis approach of a rare case of secretory carcinoma, initially diagnosed as acinic cell carcinoma, in a 33-year-old male patient. The specimen was histologically reviewed with immunohistochemical staining for S100, CK19, mammaglobin and DOG1. Afterwards fluorescence in situ hybridization (FISH) was performed to detect the ETV6-NTRK3 gene fusion, in order to recognize a secretory carcinoma. Surgery was the only treatment required in this case.

Secretory carcinoma or mammary analogue secretory carcinoma (MASC) is a rare new entity of low-grade malignant tumor of salivary glands (1).

It was recognized as a distinct entity in the recent 2017 World Health Organization (WHO) classification of salivary gland tumors (2).

More than 232 worldwide cases of secretory carcinoma have been published most of them were in the parotid gland, followed by the intraoral minor salivary glands then the submandibular gland (3). The true incidence of this entity is currently unknown due to its rarity, its recent description, its architectural variability, and its morphological similarities with other salivary gland tumors. All these factors led to diagnostic difficulties and previous misclassification of this tumor type.

MASC usually presents in adults with a mean patient age is 47 years. However, it is not unusual in pediatric populations (4). It arises equally in men and women.

The distribution of reported case of mammary analog secretory carcinoma showed a predilection in developed countries (3), it may be due to the lack of scientific research accessibility in developing countries.

Clinically, MASC presents as an asymptomatic, slow-growing mass. Macroscopic appearance shows a poorly defined and rubbery consistency, with a white tan to gray cut surfaces (5). Cyst formation with translucent yellowish gel is encountered. In our case, the palpation gave impression of a well-limited mass, which could be explained by the small size of the lesion, evoking the diagnosis of a benign accessory salivary glands tumor.

It was only after the interpretation of histological findings that the primary diagnosis of acinic cell carcinoma was made. Despite that this entity shares several morphological features with MASC, the diagnosis of secretory carcinoma was confirmed after performing immunohistochemical analysis due to the opposite staining profiles of both entities (6).

It is worth mentioning that combined immunohistochemical positivity of S-100 protein, mammaglobin and CK19 are useful for the diagnosis and differential diagnosis of MASC (7). However, they are not specific to it. It can be observed in intraductal carcinoma or polymorphous low-grade adenocarcinoma.

In the reported case, the final diagnosis was made after FISH analysis, which is currently the gold standard for confirming the diagnosis of secretory carcinoma (8).

At the present time, no specific therapy is available for patients with MASC. The mainstay treatment is complete surgical removal of the tumor. Some authors associate surgical treatment with radiotherapy and/ or chemotherapy especially in cases with metastases.

For this case, A complete surgical excision, no distant metastases and low-grade malignancy conditioned our treatment management solely to surgical approach.

As with any newly described entity, the data on MASC management, outcomes, and prognosis await further research with long-term follow up.

CONCLUSION

This paper reported a rare case of minor gland salivary neoplasm which made diagnosis confusion. Special consideration must be given to the development of mucocele as they can be a very alarming sign of a hidden malignancy as it has been reported in our case. Immunostaining and identification of the fusion gene by molecular biology revealed the real identity of this entity.

Due to the limited data available with regard to treatment protocols and prognosis, further research is substantially needed in order to establish a guideline for the clinical course, medical and surgical management, and long-term outcome.

Conflict of interest statement: The authors declare that they have no conflicts of interest, and no financial support for this article of review was required.

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